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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/597,902

08/11/2006

Brian Alvin Johns

PR60567USW

7724

513 7590 06/12/2009

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EXAMINER

O DELL, DAVID K

ART UNIT

PAPER NUMBER

1625

MAIL DATE

DELIVERY MODE

06/12/2009

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/597,902	Applicant(s) JOHNS ET AL.	
	Examiner David K. O'Dell	Art Unit 1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 19 May 2009.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 5-8, 10-21, 25-29 and 33-40 is/are pending in the application.
- 4a) Of the above claim(s) 20, 21, 28, 29, 35, 39 and 40 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 5-8, 10-19, 25-27, 33, 34 and 36-38 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. This application is a 371 of PCT/US05/04085 filed 02/10/2005, which claims benefit of 60/543,670 filed 02/11/2004.

Claims 5-8, 10-21, 25-29, 33-40 are pending. Claims 20-21, 28-29, 35, 39, 40 are withdrawn.

Request for Continued Examination

2. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on May 19, 2009 has been entered.

Claim Rejections/Objections Maintained/ New Grounds of Rejection

3. The rejection of claims 5-8, 10-19, 25-27, 33, 34, 36-38 over the judicially created doctrine of obviousness type double patenting (ODP) over 11/997,786, 11/478,218, and U.S. 7,358,249 are maintained. The examiner may be in a position to withdraw provisional rejections based on applications with a later filing date if these are the only remaining rejections, however the rejections over the '786 and '218 applications are not the only remaining rejections since the '249 patent ODP rejection is still valid and not overcome. The examiner has shown that the instant claims are obvious variants of the '249 patent. lists in the Action a number of compounds which are alleged to anticipate or render obvious the claimed compounds. Applicant has suggest that the '249 patent does not cover halogenated benzyl compounds, however the compounds of

claim 3 of the '249 are clearly halogenated, supported by species in the specification. The applicant has pointed to the proviso language of claim 5, as excluding all of the prior art species that might support the genus. Double patenting rejections are a claim by claim analysis, presumably '249 patent covers the entire genus and species a detailed analysis is not necessarily required. A claim is a group of words defining only the boundary of the patent monopoly. Can it be obvious or not obvious to modify a legal boundary? If the '249 patent is valid and according to 35 U.S.C. 282 it must be, then the compounds described by the claims must be fully enabled and described. Doubt cannot be cast on issued patents which are presumed valid (35 U.S.C. 282) and constitute a property right (35 U.S.C. 261). As such one cannot obtain two patents covering the same material.

A new rejection is made over application 12/071,807, which was filed February 26, 2008 after the FINAL rejection of December 19, 2008.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

4. Claims 5-8, 10-19, 25-27, 33, 34, 36-38 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-11, 17-19 of copending Application No. 11/997,786. The claims overlap in scope. This is a provisional obviousness-type double patenting rejection.

5. Claims 5-8, 10-19, 25-27, 33, 34, 36-38 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 5 of copending Application No. 11/478,218. The claims overlap in scope. This is a provisional obviousness-type double patenting rejection

6. Claims 5-8, 10-19, 25-27, 33, 34, 36-38 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 5, 28-33 of copending Application No. 12/071,807. The claims overlap in scope, see the Formula of claim 5, and the detailed analysis at 7 in this action as the '807 claim 5 is the same as the claim 3 of the '249 patent. This is a provisional obviousness-type double patenting rejection

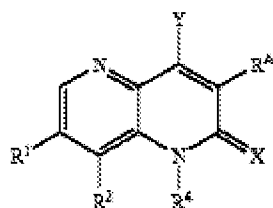
7. Claims 5-8, 10-19, 25-27, 33, 34, 36-38 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 3, 6, 12, 14 of U.S. patent 7,358,249. The claims overlap in scope. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

Determination of the scope and content of the prior art and the instant claims

(MPEP 2141.01)

The '249 patent teaches the compounds of the instant case. Claim 3 of the '249 patent is shown below:

3. The compound of claim 1, represented by the general formula (IV-2):



(IV-2) 5

6

or the pharmaceutically acceptable salt thereof;
wherein X, Y, R⁴, R¹, R² and R³ are as defined in claim 6

Where

R¹ is a group of the formula: -Z¹-Z²-Z³-R⁵
wherein
Z¹ and Z³ each are independently a single bond, optionally substituted alkylene or optionally substituted alkenylene;
Z² is a single bond, optionally substituted alkylene, optionally substituted alkenylene,

R⁴ is optionally substituted aryl,

X is oxygen,

R⁴ is -C(=Z)R⁷ wherein Z is a substituent selected from Substituent Group A, R⁷ is

-NHOH,

Y is —OH ,

R^1 each is i : substituent selected from Substituent Group A or hydrogen;
Substituent Group A is a group consisting of halogen, optionally substituted alkoxycarbonyl, carboxy, optionally substituted alkyl, optionally substituted alkoxy, alkoxyalkyl, nitro, hydroxy, hydroxyalkyl, optionally substituted alkenyl, optionally substituted alkynyl, alkylsulfonyl, alkylalkoxysulfonyl, optionally substituted amino, optionally substituted aminosulfonyl, alkylthio, alkylthioalkyl, haloalkyl, haloalkoxy, haloalkoxyalkyl, cycloalkyl, cycloalkenyl, oxo, thiono, alkylenedioxy, alkylene, alkenylene, nitroso, azido, amidino, guanidino, cyano, isocyano, mercapto, optionally substituted carbamoyl, optionally substituted carbamoylalkyl, optionally substituted sulfamoyl, sulfamino, sulfo, formyl, alkylcarbonyl, alkylcarbonyloxy, hydrazino,

morpholino, phosphono, phosphinoyl, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted heterocycle, optionally substituted aralkyl, optionally substituted heteroaralkyl, optionally substituted aryloxy, optionally substituted heteroaryloxy, optionally substituted heterocycloxy, optionally substituted arylthio, optionally substituted heteroarylthio, optionally substituted aralkyloxy, optionally substituted heteroaralkyloxy, optionally substituted aralkylthio, optionally substituted heteroaralkylthio, optionally substituted aryloxyalkyl, optionally substituted heteroaryloxyalkyl, optionally substituted arylthioalkyl, optionally substituted heteroarylthioalkyl, optionally substituted arylsulfonyl, optionally substituted heteroarylsulfonyl, optionally substituted aralkylsulfonyl, optionally substituted heteroaralkylsulfonyl, optionally substituted alkylcarbonyl alkyl, optionally substituted arylcarbonyl alkyl, alkylsulfonyloxy, sulfamoyloxy and optionally substituted arylcarbonyl;

Clearly this is nearly the same genus of instant claim 5, and such language encompasses all genera and the species of the instant claims. These compounds have exactly the same utility (HIV integrase inhibitor). While the '249 patent is broader, claim 9 points exactly to preferred R1 definitions, i.e. R1 is halobenzyl etc.

9. The compound of claim 7 or the pharmaceutically acceptable salt thereof, wherein:

R^1 is benzyl optionally substituted by halogen;

R^2 is hydrogen;

R^{10} is hydrogen, halogen, optionally substituted amino, optionally substituted alkenyl; optionally substituted alkynyl, carboxy, alkoxycarbonyl or optionally substituted carbamoyl;

R^4 is a group of the formula: $-C(=O)-R^7$ wherein R^7 is

hydroxy,

optionally substituted alkoxy,

NR^8R^9 wherein R^8 is hydrogen and R^9 is

hydrogen,

alkyl optionally substituted by alkoxy or

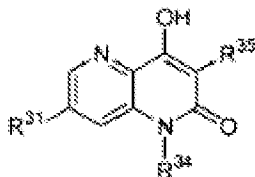
amino optionally substituted alkyl, or

optionally substituted heterocycloxy; and

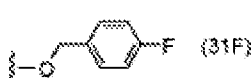
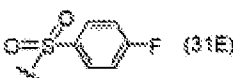
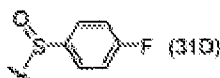
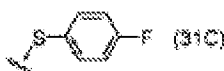
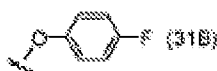
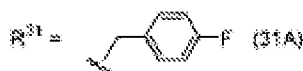
Y is hydroxy.

Claim 10 further defines the other moieties. This subgenus is directly pointed to by the preferred embodiments in the specification, i.e. where various amides were prepared, in the structures shown below

The present invention further includes the following compounds. These compounds may be synthesized in a manner similar to that of the above Examples.



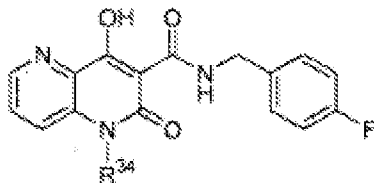
The substituents of R^{31} , R^{34} and R^{35} on the above compounds are exemplified by the following substituents:



$R^{34} =$ Me (34A), Et (34B), Pr (34C), COMe (34D), SO₂Me (34E)

$R^{35} =$ COOMe (35A), COOEt (35B), COOiPr (35C), COEt (35D), COCH₂CH₂CH₂OMe (35E), CONHMe (35F), CONHEt (35G), CONHCH₂CH₂OMe (35H)

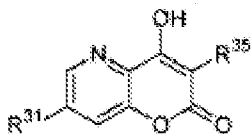
R^{34} is 34A and R^{35} is 35A. Other combinations are also shown in a similar manner.



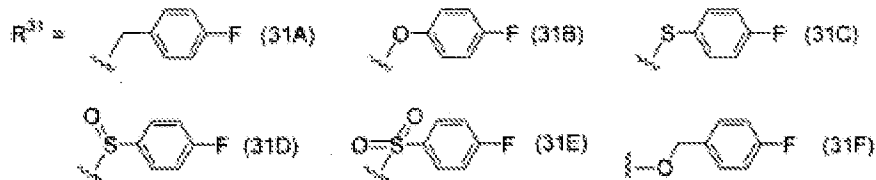
The substituent of R^{35} on the above compound includes the following:

R^{34} = Me (34A), Et (34B), Pr (34C), COMe (34D), SO₂Me (34E)

The present invention includes the following compounds. These compounds may be synthesized in a manner similar to that of above Examples.



The substituents of R^{31} and R^{35} on the above compounds are exemplified by the following substituents:



R^{35} = COOMe (35A), COOEt (35B), COOPr (35C), COEt (35D), COCH₂CH₂CH₂OMe (35E), CONHMe (35F), CONHEt (35G), CONHCH₂CH₂OMe (35H)

The preferable combinations of substituents (shown in the order of (R^{31} , R^{35})) involve the followings:

(31A, 35A), (31A, 35B), (31A, 35C), (31A, 35D), (31A, 35E), (31A, 35F), (31A, 35G), (31A, 35H), (31B, 35A), (31B, 35B), (31B, 35C), (31B, 35D), (31B, 35E), (31B, 35F), (31B, 35G), (31B, 35H), (31C, 35A), (31C, 35B), (31C, 35C), (31C, 35D), (31C, 35E), (31C, 35F), (31C, 35G), (31C, 35H), (31D, 35A), (31D, 35B), (31D, 35C), (31D, 35D), (31D, 35E), (31D, 35F), (31D, 35G), (31D, 35H), (31E, 35A), (31E, 35B), (31E, 35C), (31E, 35D), (31E, 35E), (31E, 35F), (31E, 35G), (31E, 35H), (31F, 35A), (31F, 35B), (31F, 35C), (31F, 35D), (31F, 35E), (31F, 35F), (31F, 35G), (31F, 35H)

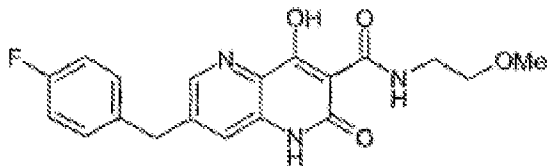
For Examples: (R^{31} , R^{35}) = (31A, 35A) means a compound wherein R^{31} is 31A; and R^{35} is 35A. Other combinations are also shown in a similar manner.

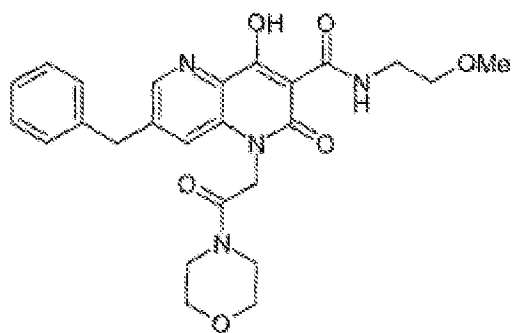
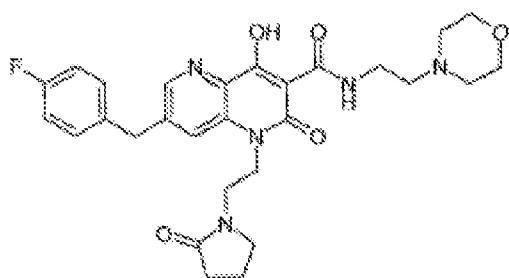
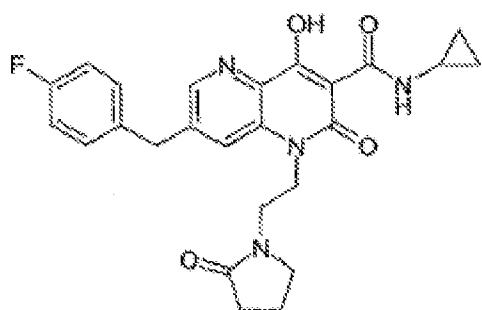
Ascertainment of the difference between the prior art and the claims

(MPEP 2141.02)

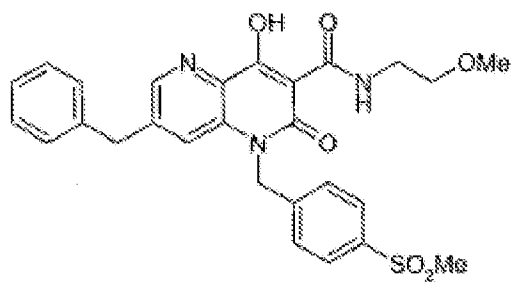
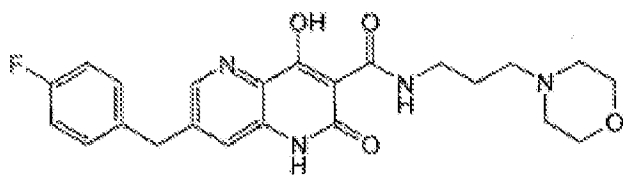
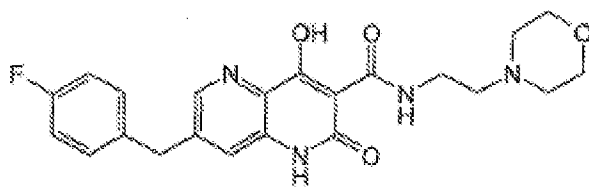
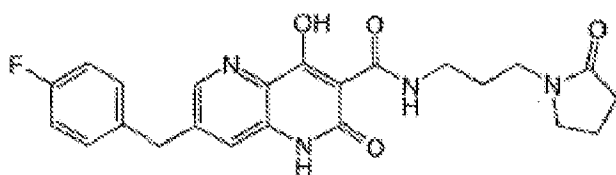
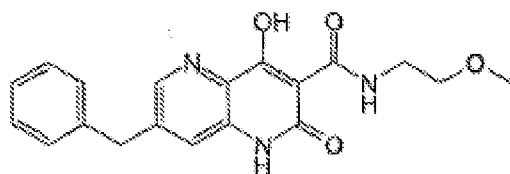
Comparing the instantly claimed preferred compounds (those with biological data), Below:

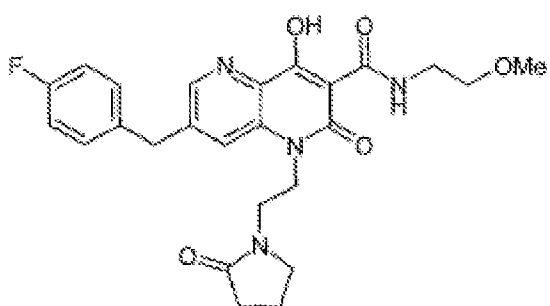
Example 2



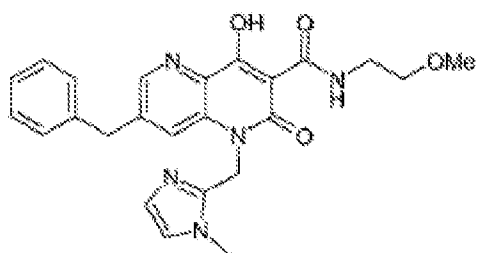


Example 17:

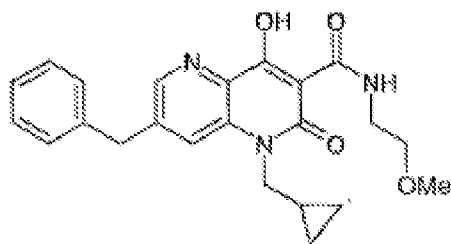




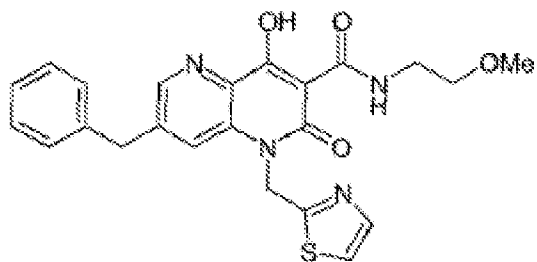
Example 50:



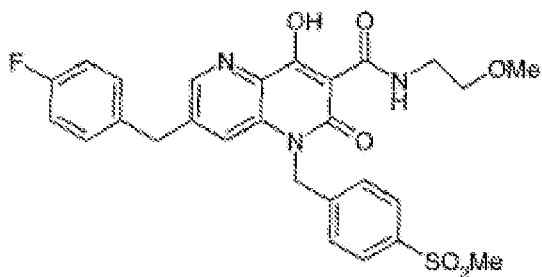
Example 54:



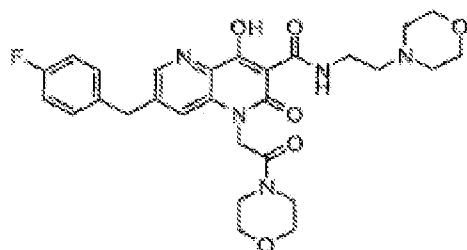
Example 62:



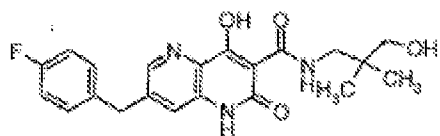
Example 64:



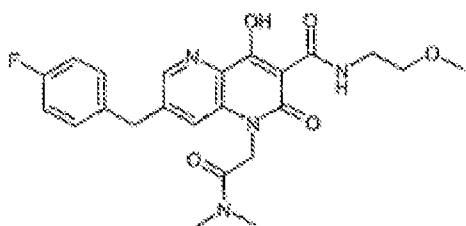
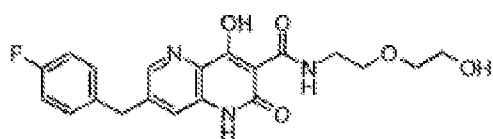
Example 83:



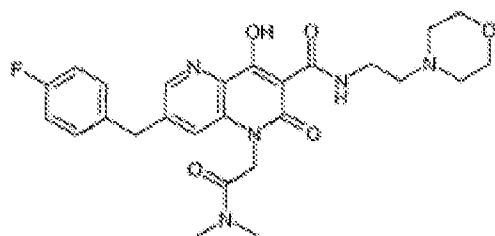
Example 85:



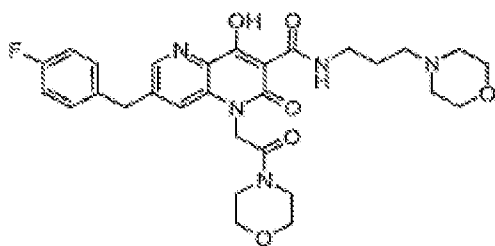
Example 86:



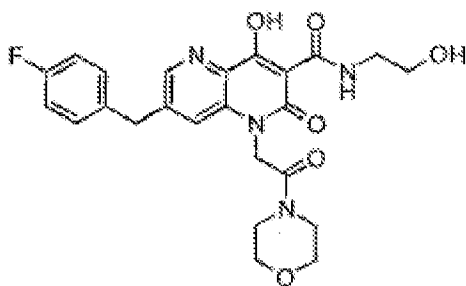
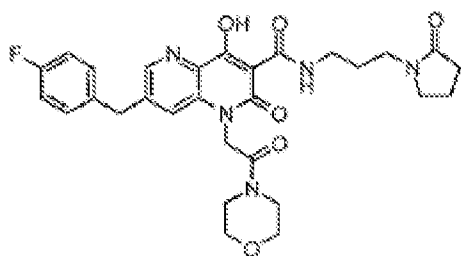
Example 91:



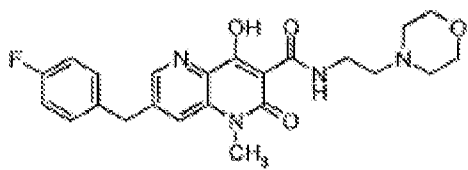
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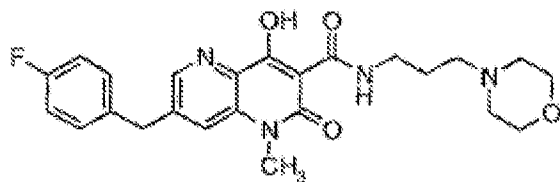


Example 94:

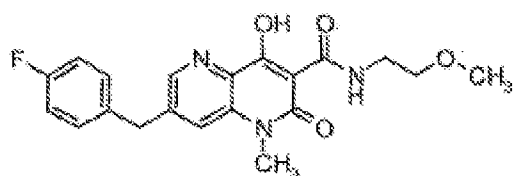


Example 96:

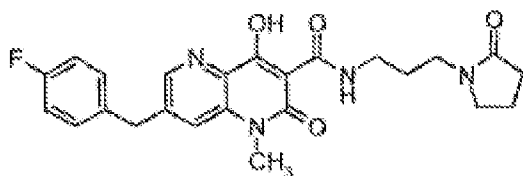




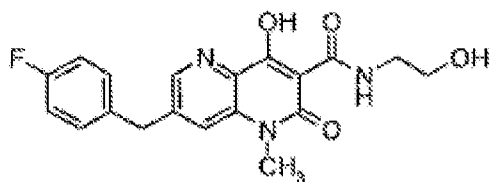
Example 98:



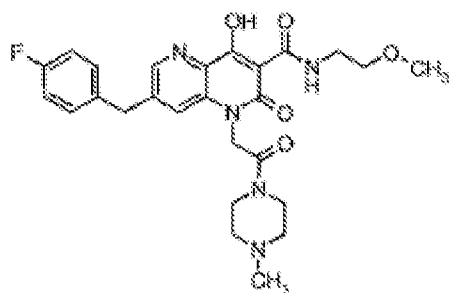
25 Example 99:



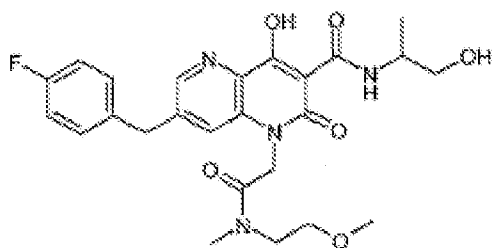
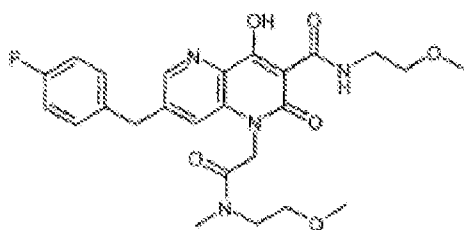
Example 101:



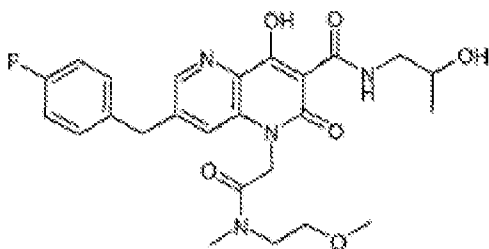
Example 102:



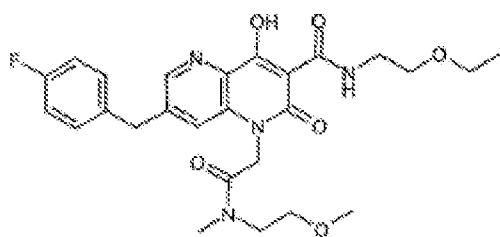
Example 104:



Example 106:



Example 107:



It is clear that all these substitutions were within the teaching of the claimed invention in the '249 patent, in particular when the various preferred moieties are considered (i.e. claim 10 of the '249 patent). Some of the species of the '249 patent would read directly on the claims, except the claim 5 has some proviso.

Finding of prima facie obviousness

Rational and Motivation

(MPEP 2142-2143)

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to make compounds of the '249 patent to produce the instant invention. The

experienced Ph.D. synthetic organic chemist, who would make Applicants' compounds, would be motivated to prepare these compounds on the expectation that anticipatory compounds or analogues falling within the general teaching would have similar properties and upon the routine nature of such experimentation in the art of medicinal chemistry.

A reference is good not only for what it teaches by direct anticipation but also for what one of ordinary skill in the art might reasonably infer from the teachings. (*In re Opprecht* 12 USPQ 2d 1235, 1236 (Fed Cir. 1989); *In re Bode* 193 USPQ 12 (CCPA) 1976). In light of the forgoing discussion, the Examiner concludes that the subject matter defined by the instant claims would have been obvious within the meaning of 35 USC 103(a). From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

One of ordinary skill is also one of "ordinary creativity, not an automaton". See *Leapfrog Enterprises Inc. v. Fisher-Price. and Mattel Inc.* UNITED STATES COURT OF APPEALS FOR THE FEDERAL CIRCUIT "An obviousness determination is not the result of a rigid formula disassociated from the consideration of the facts of a case. Indeed, the common sense of those skilled in the art demonstrates why some combinations would have been obvious where others would not. See *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. , 2007 U.S. LEXIS 4745, 2007 WL 1237837, at 12 (2007) ("The combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results.").

Moreover since the '249 patent covers the entire genus and species a detailed analysis is not necessarily required. A claim is a group of words defining only the boundary of the patent monopoly. Can it be obvious or not obvious to modify a legal boundary? If the '249 patent is valid and according to 35 U.S.C. 282 it must be, then the compounds described by the claims must be fully enabled and described. Doubt cannot be cast on issued patents which are presumed valid (35 U.S.C. 282) and constitute a property right (35 U.S.C. 261). As such one cannot obtain two patents covering the same material.

Conclusion

8. All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David K. O'Dell whose telephone number is (571)272-9071. The examiner can normally be reached on Mon-Fri 7:30 A.M.-5:00 P.M EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached on (571)272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

D.K.O.

/Rita J. Desai/

Primary Examiner, Art Unit 1625